NARCOTIC ACTION OF HEXOBARBITAL WHEN GIVEN TOGETHER WITH RADIOPROTECTORS OF THE AMINOTHIOL SERIES TO IRRADIATED ANIMALS

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In experiments on mice hexobarbital, alone and together with β-mercaptopropylamine, cystamine hydrochloride, and cystamine hydrobromide, was injected 1.5-2 h after irradiation of the animals with γ-rays (dose 900 R). All three radioprotectors were shown to potentiate the narcotic action of hexobarbital (by 2.8-7 times in unirradiated and 6.8-17.7 times in irradiated mice compared with the corresponding control). The longest narcotic effect was observed as a result of the combined administration of hexobarbital and cystamine hydrobromide.

The response of the irradiated organism to narcotics is dependent to a certain extent on the chemical structure of the compound, the severity of the radiation injury, and the period of development of radiation sickness. For example, the narcotic effect of barbiturates during the first hours after general exposure to ionizing radiation, producing acute radiation sickness of the IInd-IIIrd degree, is weakened. However, the toxic effect of these narcotics is not only not reduced but is even potentiated. In the initial period of radiation sickness and, in particular, at its height, sensitivity to barbiturates is considerably increased [1-5].

It has also been shown experimentally that many radioprotectors and, in particular, those of the aminothiol group may considerably potentiate the narcotic effect of general anesthetics and, in particular, of barbiturates [6].

However, no experimental data relating to the potentiating action of radioprotectors on the narcotic effect of general anesthetics in radiation sickness can be found in the literature.

It was therefore decided to investigate the action of hexobarbital in combination with radioprotectors in irradiated animals.

EXPERIMENTAL METHOD

Experiments were carried out on 643 noninbred male albino mice weighing 20-22 g. The mice were irradiated with a Co^{60} γ-ray apparatus in a dose of 900 R. This dose is the minimal absolutely lethal dose for mice. The solution of hexobarbital and solution of hexobarbital with the radioprotector were prepared immediately before use and injected intraperitoneally 1.5-2 h after irradiation in the following doses: hexobarbital 75 mg/kg, β-mercaptopropylamine (MPA), cystamine hydrochloride, and cystamine hydrobromide—100 mg/kg each (calculated as the salt). The narcotic effect was estimated from the time of onset and duration of the lateral position.

EXPERIMENTAL RESULTS

The results (Table 1) show that all three radioprotectors potentiated the narcotic action of hexobarbital (by 2.8-7 times in the unirradiated and 6.8-17.7 times in the irradiated animals compared with the

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TABLE 1. Duration of Narcotic Effect of Hexobarbital Combined with Radioprotectors in Irradiated and Unirradiated Animals

Preparation	Dose of irradiation (in R)	Number of mice	Number of mice developing narcosis (in %)	Mean duration of lateral position (in min)
Hexobarbital	—	68	61,8	10,2±1,2
Hexobarbital + Cystamine hydrochloride	—	70	94,3	44,8±9,2*
Hexobarbital	900	60	15,8	3,5±0,6
Hexobarbital + Cystamine hydrochloride	900	60	90,0	32,6±8,2*
Hexobarbital	—	45	50,0	12,6±1,6
Hexobarbital + Cystamine hydrobromide	—	50	100,0	88,4±10,2*
Hexobarbital	900	50	16,0	2,8±0,3
Hexobarbital + Cystamine hydrobromide	900	50	100,0	49,6±8,9*
Hexobarbital	—	45	53,0	12,7±1,3
Hexobarbital + Dose of irradiation (in R)	—	45	88,9	36,6±4,7*
Hexobarbital	900	50	18,0	4,6±0,6
Hexobarbital + Dose of irradiation (in R)	900	50	88,0	31,3±6,6*

*P < 0.05 compared with the corresponding control.

corresponding control), and considerably increased the length of time spent by the animals in the lateral position. No significant difference was found in the time of its onset, but the period of excitation was less marked in the mice receiving hexobarbital combined with the radioprotectors. The most prolonged narcotic effect was observed after the combined administration of hexobarbital and cystamine hydrobromide.

In the writers' opinion these results are of considerable practical importance in surgery. It must also be remembered that the aminothiols reduce vascular permeability, decrease the blood clotting time, and may have a beneficial effect on the course and outcome of acute radiation sickness.

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